

explanation of the relevance of EP 0 088 046 and EP 0 133 988 (references BF and BG in the originally filed PTO-1449), as it is presently understood by the individual designated in 37 C.F.R. § 1.56(c) most knowledgeable about the content of each patent. In addition, the substitute PTO-1449 has been amended to remove reference to EP 0 143 949 (reference BH in the originally filed PTO-1449), since this reference was cited twice (*see* reference BC). Finally, the substitute PTO-1449 was amended to remove reference to *Current Protocols In Molecular Biology* (Ausubel *et al.*, eds., John Wiley & Sons 1994); *Remington's Pharmaceutical Sciences* (Gennaro, ed., Mack Publishing 18th ed. 1990); *Computer Analysis of Sequence Data*, Part 1 (Griffin *et al.*, eds., Humana Press 1994); *Sequence Analysis Primer* (Gribskov *et al.*, eds., Oxford University Press 1991); von Heinje, *Sequence Analysis in Molecular Biology* (Academic Press 1987); *Computational Molecular Biology* (Lesk, ed., Oxford University Press 1998); Sambrook, *Molecular Cloning: A Laboratory Manual* (Cold Springs Harbor University Press 1989), *Biocomputing: Informatics and Genome Projects* (Smith, ed., Academic Press 1993); and Steward *et al.*, *Solid Phase Peptide Synthesis* (W.H. Freeman & Co. 1984) (references CC, DL, DM, DO, DP, EA, EL, EN, and EO, respectively, in the originally filed PTO-1449). As these references merely reflect the general state of the art at the time the invention was made, Applicants are unable to specifically indicate or provide copies of the relevant pages.

2. Objection to claims 1-8, 10, 11, 46-48, and 55

The Office Action contains an objection to claims 1-8, 10, 11, 46-48, and 55 as being improperly dependent because the claims are dependent upon a non-elected invention. Applicants have amended claims 1-3 to recite only the elected invention.

3. Objection to specification

The Office Action contains an objection to the specification for containing a space on page 106 between the terms "intracerebral" and "(intra-parenchymal)." Applicants note that there is only a single space between these terms, and that the seemingly irregular spacing is due to the length of the term (*i.e.*, "intracerebroventricular") that immediately follows the term "(intra-parenchymal)."

4. Rejections of claims 1-8, 10, 11, 46-48, and 55 under 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 1-8, 10, 11, 46-48, and 55 under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims. The Examiner takes the position that the as-filed specification contemplates several methods of gene therapy using the polynucleotides of the claimed invention, and that it would require undue experimentation to determine how to use these polynucleotides in any method of gene therapy.

First, Applicants disagree with the Examiner's assertion that "the elected invention lies in the field of gene therapy" (p. 4 of Office Action). Applicants contend that the pending claims are directed instead to B7-like nucleic acid molecules. Applicants further contend that the B7-like nucleic acid molecules of the claimed invention are enabled for use in, for example, drug candidate screening assays. Specifically, the instant specification provides the nucleotide sequences of a number of B7-like nucleic acid molecules (e.g., SEQ ID NO: 2, SEQ ID NO: 4, and SEQ ID NO: 6), methods for making a transgenic mouse using the claimed B7-like nucleic acid molecules (section entitled "Genetically Engineered Non-Human Animals" beginning at page 74), and guidance for using the transgenic animals of the present invention to screen for drug candidates (p. 75, ln. 7-28). In view of this disclosure, Applicants contend that the instant specification is enabling for use of the invention commensurate in scope with the claims (*i.e.*, B7-like nucleic acid molecules).

In order to provide a reply to the instant Office Action that is fully responsive, Applicants now turn to the particular rejections asserted in the Office Action. The Examiner first asserts that the specification does not enable claims directed to a method of modulating levels of a polypeptide in an animal comprising administering to the animal the nucleic acid molecule of any of Claims 1, 2, or 3, because the claimed invention does not specify the polypeptide in the animal to be modulated. Applicants have amended Claim 55 to indicate that the polypeptide to be modulated is a "B7-like polypeptide." The specification defines the term B7-like polypeptide at page 16, line 23 to page 17, line 3. Applicants respectfully contend that this ground of rejection has been overcome by amendment.

The Examiner next asserts that the specification does not enable claims to a pharmaceutical

composition comprising a nucleic acid molecule of Claims 1, 2, or 3. In order to expedite prosecution of the instant application, Applicants have canceled claims 46 and 47 without prejudice or disclaimer, rendering this ground of rejection moot. This amendment has been made solely to expedite prosecution and was not made to overcome prior art.

The Examiner also takes the position that it would require undue experimentation to determine the genetic sequences embraced by the claims of the instant application. The Examiner first asserts that it would not be apparent to one of ordinary skill in the art that nucleic acid molecules encoding a polypeptide having a substitution and/or deletion of 1 to 100 amino acid residues in the polypeptide set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 would have B7-like polypeptide activity. Applicants have deleted Claim 2(g) of the as-filed specification, rendering this ground of rejection moot. The Examiner next asserts that it would not be apparent to one of ordinary skill in the art how nucleotide sequences complementary to the nucleotide sequences of SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5 would exhibit B7-like polypeptide activity. Applicants contend that Claims 1(e), 2(k), and 3(l) of the as-filed specification are directed to nucleotide sequences that hybridize to nucleotide sequences that are complementary to the nucleotide sequences of the present invention, and are *not themselves* complementary to the nucleotide sequences of the present invention. Applicants therefore assert that it would be apparent to one with skill in the art how the nucleotide sequences of Claims 1(e), 2(k), and 3(l) would exhibit B7-like polypeptide activity, and respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment, traversed by argument, or mooted by cancellation of the rejected claims, and request that the Examiner withdraw all rejections made on this basis.

5. Rejections of claims 1-3, 8, 10, and 47 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 1-3, 8, 10, and 47 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner takes the position that claims 1-3 are indefinite because the phrase “moderately or highly stringent conditions” is not defined by the claims and the specification does not provide a standard for ascertaining the

parameters of such conditions. Applicants note that definitions of "moderately stringent conditions" and "highly stringent conditions" are provided in the specification at page 29, lines 4-13 and page 27, lines 13-24, respectively. As an Applicant is entitled to be his or her own lexicographer, these definitions control the interpretation of the phrase "moderately or highly stringent conditions" as it is used in the claims of the instant application, provided that these definitions are not contrary to the meanings of these terms in the art. Moreover, Applicants contend that it would be apparent to one of ordinary skill in the art, in view of the teachings in the instant specification, whether a particular set of hybridization conditions was either "moderately stringent" or "highly stringent." Therefore, Applicants contend that the claims are not indefinite for reciting the phrase "moderately stringent conditions," and respectfully request withdrawal of this ground of rejection.

The Examiner also takes the position that claims 8 and 10 are indefinite because the phrase "B7-like polypeptide" is not defined by the claims and the specification does not provide a standard for ascertaining the meaning of this phrase. Applicants note that an explicit definition of "B7-like polypeptide" is provided in the specification at page 16, line 23 to page 17, line 3, and contend that this definition controls the interpretation of the phrase "B7-like polypeptide" as it is used in the claims of the instant application. Applicants contend, for example, that it would be apparent to one of ordinary skill in the art that a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 is a B7-like polypeptide. Applicants further contend that it would be apparent to one of ordinary skill in the art that a polypeptide variant (e.g., a polypeptide having at least one conservative amino acid substitution) of the amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 is a B7-like polypeptide, provided that the polypeptide variant has an activity of the polypeptide as set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6. Therefore, Applicants contend that the claims are not indefinite for reciting the phrase "B7-like polypeptide," and respectfully request withdrawal of this ground of rejection.

The Examiner further takes the position that claim 47 is indefinite because the limitation "[a] composition of claim 46" lacks an antecedent basis. Applicants have canceled claim 47, rendering this ground of rejection moot.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been traversed by argument or mooted by cancellation of the rejected claims, and request that

the Examiner withdraw all rejections made on this basis.

8. Rejections of claims 1-3 under 35 U.S.C. § 102

The Office Action asserts a rejection of claims 1-3 under 35 U.S.C. § 102, as being anticipated by Marra *et al.* (The Washington University-NCI Mouse EST project, seq_name: gb_est82:BF040046, July 2, 1999; GenBank Accession No. AI790785), contending that Marra *et al.* disclose an EST sequence that shares 85% similarity with the nucleotide sequences set forth in SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5, and therefore would hybridize under moderately stringent conditions to nucleic acid molecules comprising these nucleotide sequences. Applicants traverse this rejection.

Marra *et al.* disclose a nucleotide sequence of 530 bp. SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5 set forth nucleotide sequences of 1146 bp, 1158 bp, and 1158 bp, respectively. Exhibits A-C indicate that there is an overlap of no more than 274 bp or 286 bp between the nucleotide sequence disclosed by Marra *et al.* and the nucleotide sequences set forth in SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5. Exhibits A-C also indicate that in the overlapping regions, the sequences share an identity of between 69.6% to 72.6%, and *not* 85% (Applicants understand the Office Action to mean 85% *identity*, rather than *similarity*, since the term “similarity” refers to the degree of sequence relatedness between two polypeptide sequences, and is defined as such in the instant specification at page 21, lines 6-20). Applicants contend that because the nucleotide sequence of Marra *et al.* and the nucleotide sequences set forth in SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5 share no more than 72.6% identity over no more than 286 bp, a nucleic acid molecule comprising the nucleotide sequence of Marra *et al.* would *not* hybridize under moderately stringent conditions to nucleic acid molecules comprising the nucleotide sequences set forth in SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5. Therefore, Applicants contend that Marra *et al.* does not anticipate claims 1-3, and respectfully request that the Examiner withdraw this rejection.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.



AMENDMENTS TO THE CLAIMS

Marked Up Versions of Amended Claims under 37 C.F.R. 1.121(c)(1)(ii)

1. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from:

- (a) the nucleotide sequence as set forth in any of SEQ ID NOs: 1, SEQ ID NO: 3, or SEQ ID NO: 5 or 7;
- _____ (b) ~~the nucleotide sequence as set forth in SEQ ID NOs: 9, 11 or 13;~~
- _____ (c) ~~(b) a nucleotide sequence encoding the polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6 or 8;~~
- _____ (d) ~~a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;~~
- _____ (e) ~~(c) a nucleotide sequence which hybridizes under at least moderately or highly stringent conditions to the complement of the nucleotide sequence of either (a) or (b), wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6 or 8; or~~
- _____ (f) ~~a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of (a) or (b), wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14; and~~
- _____ (g) ~~(d) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - (f)(c).~~

2. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from:

- (a) a nucleotide sequence encoding a polypeptide that is at least about 70, 75, 80, 85, 90, 95, 96, 97, 98 or 99 percent identical to the polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6 or 8, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6 or 8;
- _____ (b) ~~a nucleotide sequence encoding a polypeptide that is at least about 70, 75, 80, 85, 90, 95, 96, 97, 98 or 99 percent identical to the polypeptide as set forth in SEQ ID NOs: 10, 12 or 14,~~

~~wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;~~

(e)(b) ~~a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in any of SEQ ID NOs: 1, SEQ ID NO: 3, or SEQ ID NO: 5 or 7, or the nucleotide sequence of (a), wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6 or 8;~~

(d) ~~a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in SEQ ID NOs: 9, 11 or 13, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;~~

(e)(c) ~~a region of the nucleotide sequence of any of SEQ ID NOs: 1, SEQ ID NO: 3, or SEQ ID NO: 5 or 7, or the nucleotide sequence of (a) or (b), above, encoding a polypeptide fragment of at least about 25 amino acid residues, wherein the polypeptide fragment has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6 or 8, or is antigenic;~~

(f) ~~a nucleotide sequence of SEQ ID NOs: 9, 11 or 13, or (a) or (b), above, encoding a polypeptide fragment of at least about 25 amino acid residues, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;~~

(g) ~~a nucleotide sequence encoding a polypeptide that has a substitution and/or deletion of 1 to 100 amino acid residues as set forth in any of SEQ ID NOs: 1, 3, 5 or 7, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 2, 4, 6 or 8;~~

(h) ~~a nucleotide sequence encoding a polypeptide that has a substitution and/or deletion of 1 to 100 amino acid residues as set forth in any of SEQ ID NOs: 9, 11 or 13, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;~~

(i)(d) ~~a region of the nucleotide sequence of any of SEQ ID NOs: 1, SEQ ID NO: 3, or SEQ ID NO: 5 or 7, or the nucleotide sequence of any of (a), (c), (e) or (g), above, comprising a fragment of at least about 16 nucleotides;~~

(i) ~~a nucleotide sequence of SEQ ID NOs: 9, 11 or 13, or (b), (d), (f) or (h), above,~~

comprising a fragment of at least about 16 nucleotides;

(k)(e) a nucleotide sequence which hybridizes under at least moderately or highly stringent conditions to the complement of the nucleotide sequence of any of (a), (e), (e), (g) or (i) - (d), above, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOS: 2, SEQ ID NO: 4, or SEQ ID NO: 6 or 8; or

— (l) — a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (b), (d), (f), (h) or (j), above, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOS: 10, 12 or 14; and

(m)(f) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - (l)(e).

3. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from:

(a) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NOS: 2, SEQ ID NO: 4, or SEQ ID NO: 6 or 8 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOS: 2, SEQ ID NO: 4, or SEQ ID NO: 6 or 8;

— (b) — a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NOS: 10, 12 or 14 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOS: 10, 12 or 14;

(c)(b) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NOS: 2, SEQ ID NO: 4, or SEQ ID NO: 6 or 8 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOS: 2, SEQ ID NO: 4, or SEQ ID NO: 6 or 8;

— (d) — a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NOS: 10, 12 or 14 with at least one amino acid insertion, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOS: 10, 12 or 14;

(e)(c) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NOS: 2, SEQ ID NO: 4, or SEQ ID NO: 6 or 8 with at least one amino acid deletion, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOS: 2,

SEQ ID NO: 4, or SEQ ID NO: 6-or-8;

— (f) — a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14 with at least one amino acid deletion, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;

(g)(d) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or-8 which has a C- and/or N- terminal truncation, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or-8;

— (h) — a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14 which has a C- and/or N- terminal truncation, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;

(i)(e) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or-8 with at least one modification that is a-selected from at least one conservative amino acid substitution, an amino acid insertion, an amino acid deletion, C-terminal truncation, and/or N-terminal truncation, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or-8;

— (j) — a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14 with at least one modification selected from at least one amino acid substitution, amino acid insertion, amino acid deletion, C terminal truncation, and N terminal truncation, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;

(k)(f) a nucleotide sequence of any of (a) - (j)(e) comprising a fragment of at least about 16 nucleotides;

(l)(g) a nucleotide sequence which hybridizes under at least moderately or highly stringent conditions to the complement of the nucleotide sequence of any of (a), (e), (e), (g), (i) or (k) - (f), wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or-8; or

— (m) — a nucleotide sequence which hybridizes under moderately or highly stringent

~~conditions to the complement of any of (b), (d), (f), (h), (j) or (k), wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14; and~~

~~(n)(h) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - (m)(g).~~

4. (Amended) A vector comprising the nucleic acid molecule of any of Claims 1, 2, or 3.

11. (Amended) The isolated nucleic acid molecule according to Claim 2, wherein the percent identity is determined using a computer program ~~selected from that is~~ GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, ~~and~~ or the Smith-Waterman algorithm.

48. (Amended) A viral vector comprising a nucleic acid molecule of any of Claims 1, 2, or 3.

55. (Amended) A method of modulating levels of a B7-like polypeptide in an animal comprising administering to the animal the nucleic acid molecule of any of Claims 1, 2, or 3.



EXHIBIT A

	10	20	30	40	50	60	
SEQ01_ORF	*	*	*	*	*	*	*
	ATGGGGCTTG	TGATTTCCCT	CCACGGTTCT	GGGTCTGGTA	ATGAAGTCAT	AGAAGGCC	
	TACCCCGAAC	ACTAAAAGGA	GGTCCAAGA	CCCAGACCAT	TACTTCAGTA	TCTTCCGGGG	
	260	270	280	290	300	310	
Marra EST	cTGGtcaTcc	TGgcTcagCT	gacaGcTTCc	GGaTCcaGTt	ATcAgaTCAT	AGAAGGtCCt>	
SEQ01_ORF	ATGGGGCTTG	TGATTTCCCT	CCACGGTTCT	GGGTCTGGTA	ATGAAGTCAT	AGAAGGCC	
	70	80	90	100	110	120	
SEQ01_ORF	*	*	*	*	*	*	*
	CAGAATGCAA	CAGTCCTGAA	GGGCTCCAG	GCTCGCTTC	ACTGCACCGT	CTCCCAGGGC	
	GTCTTACGTT	GTCAGGACTT	CCCGAGGGTC	CGAGCGAAGT	TGACGTGGCA	GAGGGTCCCG	
	320	330	340	350	360	370	
Marra EST	CAGAATGtAA	CAGTCCTaAA	GGaCTCagAG	GCTCaCTTCA	ACTGCACCGT	gaCtCAcGGC>	
SEQ01_ORF	CAGAATGCAA	CAGTCCTGAA	GGGCTCCAG	GCTCGCTTC	ACTGCACCGT	CTCCCAGGGC	
	130	140	150	160	170	180	
SEQ01_ORF	*	*	*	*	*	*	*
	TGGAAGCTCA	TCATGTGGGC	TCTCAGTGAC	ATGGTGGTGC	TAAGCGTCAG	GCCCATGGAG	
	ACCTTCGAGT	AGTACACCCG	AGAGTCACTG	TACCACCACG	ATTCGCAGTC	CGGGTACCTC	
	380	390	400	410	420	430	
Marra EST	TGGAAGCTtc	TCATGTGGaC	TCTtAaccAa	ATGGTGGTGC	TgAGtCTCcc	aCCCAaGG-a>	
SEQ01_ORF	TGGAAGCTCA	TCATGTGGGC	TCTCAGTGAC	ATGGTGGTGC	TAAGCGTCAG	GCCCATGGAG	
	190	200	210	220	230	240	
SEQ01_ORF	*	*	*	*	*	*	*
	CCCATCATCA	CCAATGACCG	CTTCACCTCT	CAGAGGTACG	ACCAGGGCGG	GAACTTCAC	
	GGGTAGTAGT	GGTTACTGGC	GAAGTGGAGA	GTCTCCATGC	TGGTCCCGCC	CTTGAAGTGG	
	440	450	460	470	480	490	
Marra EST	CCCATCATCA	CCAACaaACCG	tTTCACCTaT	gccAGtTA-c	AaCAGcatGa	cAgCTTCAtC>	
SEQ01_ORF	CCCATCATCA	CCAATGACCG	CTTCACCTCT	CAGAGGTACG	ACCAGGGCGG	GAACTTCAC	
	250	260	270	280	290	300	
SEQ01_ORF	*	*	*	*	*	*	*
	TCGGAGATGA	TCATCCACAA	TGTGGAGCCC	AGTGATTTCGG	GGAACATCAG	ATGCAGCCTC	
	AGCCTCTACT	AGTAGGTGTT	ACACCTCGGG	TCACTAAGCC	CCTTGTAGTC	TACGTGGAG	
	500	510	520				
Marra EST	TCGGAGtTGA	TCATCCAtgA	TGTGcAGCCC	AGTG>			
SEQ01_ORF	TCGGAGATGA	TCATCCACAA	TGTGGAGCCC	AGTG			

SEQ01_ORF	310	320	330	340	350	360
	*	*	*	*	*	*
	CAGAACAGTC	GCCTGCATGG	ATCTGCTTAC	CTTACCGTCC	AAGTTATGGG	AGAGCTGTTC
	GTCTTGTCA	CGGACGTACC	TAGACGAATG	GAATGGCAGG	TTCAATACCC	TCTCGACAAG
SEQ01_ORF	370	380	390	400	410	420
	*	*	*	*	*	*
	ATTCCCAGTG	TTAATCTTGT	AGTCGCTGAG	AATGAACCTT	GTGAAGTTAC	TTGTCTACCC
	TAAGGGTCAC	AATTAGAAC	TCAGCGACTC	TTACTTGAA	CACTTCAATG	AACAGATGGG
SEQ01_ORF	430	440	450	460	470	480
	*	*	*	*	*	*
	TCACACTGGA	CCCGGCTCCC	GGATATTTCC	TGGGAGCTCG	GTCTCCTGGT	CAGCCATTCA
	AGTGTGACCT	GGGCCGAGGG	CCTATAAAGG	ACCCTCGAGC	CAGAGGACCA	GTCGGTAAGT
SEQ01_ORF	490	500	510	520	530	540
	*	*	*	*	*	*
	AGCTATTATT	TTGTTCCGGA	GCCCAGCGAC	CTTCAAAGTG	CAGTGAGCAT	CCTGGCTCTG
	TCGATAATAA	AACAAGGCCT	CGGGTCGCTG	GAAGTTTCAC	GTCACTCGTA	GGACCGAGAC
SEQ01_ORF	550	560	570	580	590	600
	*	*	*	*	*	*
	ACCCCACAGA	GCAATGGGAC	TTTGACTTGC	GTGGCTACCT	GGAAGAGCCT	GAAGGCCCGC
	TGGGGTGTCT	CGTTACCCTG	AAACTGAACG	CACCGATGGA	CCTTCTCGGA	CTTCCGGGCG
SEQ01_ORF	610	620	630	640	650	660
	*	*	*	*	*	*
	AAGTCTGCAA	CTGTAAATCT	CACTGTGATT	CGGTGTCCCC	AAGACACTGG	AGGTGGTATT
	TTCAGACGTT	GACATTAGA	GTGACACTAA	GCCACAGGGG	TTCTGTGACC	TCCACCATAA
SEQ01_ORF	670	680	690	700	710	720
	*	*	*	*	*	*
	AATATTCCAG	GTGTATTATC	AAGTTTACCG	AGTTTAGGTT	TTTCATGCC	TACTTGGGGC
	TTATAAGGTC	CACATAATAG	TTCAAATGGC	TCAAATCCAA	AAAGTAACGG	ATGAACCCCG
SEQ01_ORF	730	740	750	760	770	780
	*	*	*	*	*	*
	AAAGTTGGAC	TTGGACTAGC	AGGCACCATG	CTTCTGACGC	CGACGTGTAC	TCTTACAATA
	TTTCAACCTG	AACCTGATCG	TCCGTGGTAC	GAAGACTGCG	GTCACCATG	AGAATGTTAT
SEQ01_ORF	790	800	810	820	830	840
	*	*	*	*	*	*
	CGCTGCTGCT	GCTGCCGCCG	TCGTTGTTGT	GGCTGCAACT	GCTGCTGCCG	TTGTTGTTTC
	GCGACGACGA	CGACGCCGGC	AGCAACAACA	CCGACGTTGA	CGACGACGGC	AACACAAAG
SEQ01_ORF	850	860	870	880	890	900
	*	*	*	*	*	*
	TGCTGTAGAA	GAAAAAGAGG	ATTCGTATT	CAATTCAA	AGAAATCTGA	AAAAGAGAAG
	ACGACATCTT	CTTTTCTCC	TAAAGCATAA	GTAAAGTTT	TCTTTAGACT	TTTTCTCTTC

	910	920	930	940	950	960
SEQ01_ORF	*	*	*	*	*	*
	970	980	990	1000	1010	1020
SEQ01_ORF	*	*	*	*	*	*
	1030	1040	1050	1060	1070	1080
SEQ01_ORF	*	*	*	*	*	*
	1090	1100	1110	1120	1130	1140
SEQ01_ORF	*	*	*	*	*	*
	*					
SEQ01_ORF	GTAGTA					
	CATCAT					



EXHIBIT B

	10	20	30	40	50	60	
SEQ03_ORF	*	*	*	*	*	*	*
	ATGGTGGCAG	GAGCCATGGA	AAATAGAGAC	CCACCCGGTT	CTGGGTCTGG	TAATGAAGTC	
	TACCACCGTC	CTCGGTACCT	TTTATCTCTG	GGTGGGCCAA	GACCCAGACC	ATTACTTCAG	
	260	270	280	290	300		
Marra EST	gTGcTG--gt	cAtC-cTG--	-gc-tcA-gC	tg-aCaGcTT	CcGGaTCcaG	TtATcAgaTC>	
SEQ03_ORF	ATGGTGGCAG	GAGCCATGGA	AAATAGAGAC	CCACCCGGTT	CTGGGTCTGG	TAATGAAGTC	
	70	80	90	100	110	120	
SEQ03_ORF	*	*	*	*	*	*	*
	ATAGAAAGGCC	CCCAAAATGC	AAGAGTCCTG	AAGGGCTCCC	AGGCTCGCTT	CAACTGCACC	
	TATCTTCCGG	GGGTTTTACG	TTCTCAGGAC	TTCCCGAGGG	TCCGAGCGAA	GTGACGTTGG	
	310	320	330	340	350	360	
Marra EST	ATAGAAAGGtC	CtCAgAATGt	AAcAGTCCTa	AAGGAGTCAG	AGGCTCaCTT	CAACTGCACC>	
SEQ03_ORF	ATAGAAAGGCC	CCCAAAATGC	AAGAGTCCTG	AAGGGCTCCC	AGGCTCGCTT	CAACTGCACC	
	130	140	150	160	170	180	
SEQ03_ORF	*	*	*	*	*	*	*
	GTCTCCCAGG	GCTGGAAAGCT	CATCATGTGG	GCTCTCAGTG	ACATGGTGGT	GCTAAGCGTC	
	CAGAGGGTCC	CGACCTTCGA	GTAGTACACC	CGAGAGTCAC	TGTACCACCA	CGATTGCGAG	
	370	380	390	400	410	420	
Marra EST	GTgaCtCACG	GCTGGAAAGCT	tcTCATGTGG	aCTCTtAacc	AaATGGTGGT	GCTgAGtCtC>	
SEQ03_ORF	GTCTCCCAGG	GCTGGAAAGCT	CATCATGTGG	GCTCTCAGTG	ACATGGTGGT	GCTAAGCGTC	
	190	200	210	220	230	240	
SEQ03_ORF	*	*	*	*	*	*	*
	AGGCCCATGG	AGCCCATCAT	CACCAATGAC	CGCTTCACCT	CTCAGAGGTA	CGACCAGGGC	
	TCCGGGTACC	TCGGGTAGTA	GTGGTTACTG	GCAGAAGTGGA	GAGTCTCCAT	GCTGGTCCCG	
	430	440	450	460	470	480	
Marra EST	ccaCCCAGG	-aCCCATCAT	CACCAAAcAAC	CGtTTCACCT	aTgcccAGtTA	-cAaCAGcat>	
SEQ03_ORF	AGGCCCATGG	AGCCCATCAT	CACCAATGAC	CGCTTCACCT	CTCAGAGGTA	CGACCAGGGC	
	250	260	270	280	290	300	
SEQ03_ORF	*	*	*	*	*	*	*
	GGGAACCTCA	CCTCGGAGAT	GATCATCCAC	AATGTGGAGC	CCAGTGATTC	GGGAAACATC	
	CCCTTGAAGT	GGAGCCTCTA	CTAGTAGGTG	TTACACCTCG	GGTCACTAAG	CCCCTTGTAG	
	490	500	510	520			
Marra EST	GacAgCTTCA	tCTCGGAGtT	GATCATCCAt	gATGTGcAGC	CCAGTG>		
SEQ03_ORF	GGGAACCTCA	CCTCGGAGAT	GATCATCCAC	AATGTGGAGC	CCAGTG		

SEQ03_ORF	310	320	330	340	350	360
	*	*	*	*	*	*
	AGATGCAGCC	TCCAGAACAG	TCGCCTGCAT	GGATCTGCTT	ACCTTACCGT	CCAAGTTATG
	TCTACGTCGG	AGGTCTTGTC	AGCGGACGTA	CCTAGACGAA	TGGAATGGCA	GGTTCAATAC
SEQ03_ORF	370	380	390	400	410	420
	*	*	*	*	*	*
	GGAGAGCTGT	TCATTCCCAG	TGTTAATCTT	GTAGTCGCTG	AGAATGAACC	TTGTGAAGTT
	CCTCTCGACA	AGTAAGGGTC	ACAATTAGAA	CATCAGCGAC	TCTTACTTG	AACACTTCAA
SEQ03_ORF	430	440	450	460	470	480
	*	*	*	*	*	*
	ACTTGTCTAC	CCTCACACTG	GACCTGGCTC	CCGGATATT	CCTGGGAGCT	CGGTCTCCTG
	TGAACAGATG	GGAGTGTGAC	CTGGACCGAG	GGCCTATAAA	GGACCCCTCGA	GCCAGAGGAC
SEQ03_ORF	490	500	510	520	530	540
	*	*	*	*	*	*
	GTCAGCCATT	CAAGCTATTA	TTTTGTTCCG	GAGCCCAGCG	ACCTTCAAAG	TGCACTGAGC
	CAGTCGGTAA	GTTCGATAAT	AAAACAAGGC	CTCGGGTCGC	TGGAAGTTTC	ACGTCACTCG
SEQ03_ORF	550	560	570	580	590	600
	*	*	*	*	*	*
	ATCCTGGCTC	TGACCCCACA	GAGCAATGGG	ACTTTGACTT	CGGTGGCTAC	CTGGAAGAGC
	TAGGACCGAG	ACTGGGGTGT	CTCGTTACCC	TGAAACTGAA	CGCACCGATG	GACCTTCTCG
SEQ03_ORF	610	620	630	640	650	660
	*	*	*	*	*	*
	CTGAAGGCC	GCAAGTCTGC	AACGTAAAT	CTCACTGTGA	TTCGGTGTCC	CCAAGACACT
	GACTTCCGGG	CGTTCAGACG	TTGACATT	GAGTGACACT	AAGCCACAGG	GGTTCTGTGA
SEQ03_ORF	670	680	690	700	710	720
	*	*	*	*	*	*
	GGAGGTGGTA	TTAATATTCC	AGGTGTATT	TCAAGTTAC	CGAGTTAGG	TTTTTCATTG
	CCTCCACCAT	AATTATAAGG	TCCACATAAT	AGTTCAAATG	GCTCAAATCC	AAAAAGTAAC
SEQ03_ORF	730	740	750	760	770	780
	*	*	*	*	*	*
	CCTACTTGGG	GCAAAGTTGG	ACTTGGACTA	GCAGGCACCA	TGCTTCTGAC	GCCGACGTGT
	GGATGAACCC	CGTTTCAACC	TGAACCTGAT	CGTCGTGGT	ACGAAGACTG	CGGCTGCACA
SEQ03_ORF	790	800	810	820	830	840
	*	*	*	*	*	*
	ACTCTTACAA	TACGCTGCTG	CTGCTGCCGC	CGTCGTTGTT	GTGGCTGCAA	CTGCTGCTGC
	TGAGAATGTT	ATGCGACGAC	GACGACGGCG	GCAGCAACAA	CACCGACGTT	GACGACGACG
SEQ03_ORF	850	860	870	880	890	900
	*	*	*	*	*	*
	CGTTGTTGTT	TCTGCTGTAG	AAGAAAAAGA	GGATTCGTA	TTCAATTCA	AAAGAAATCT
	GCAACAACAA	AGACGACATC	TTCTTTTCT	CCTAAAGCAT	AAGTAAAGT	TTTCTTTAGA

910 * * 920 * * 930 * * 940 * * 950 * * 960 * *
SEQ03_ORF GAAAAAGAGA AGACAAACAA AGAAACTGAG ACAGAAAGTG GAAATGAAAA CTCCGGCTAC
CTTTTCTCT TCTGTTGTT TCTTGACTC TGTCTTCAC CTTTACTTT GAGGCCGATG

970 * * 980 * * 990 * * 1000 * * 1010 * * 1020 * *
SEQ03_ORF AATTCAAGATG AACAAAAGAC CACAGACACC GCTTCTCTCC CTCCCCAAATC CTGTGAATCC
TTAAGTCTAC TTGTTTCTG GTGTCTGTGG CGAAGAGAGG GAGGGTTAG GACACTTAGG

1030 * * 1040 * * 1050 * * 1060 * * 1070 * * 1080 * *
SEQ03_ORF AGTGATCCTG AACAAAGAAA CAGTAGCTGT GGCCCTCCTC ACCAGCGGGC TGATCAACGT
TCACTAGGAC TTGTTTCTTT GTCATCGACA CCGGGAGGAG TGGTCGCCCG ACTAGTTGCA

1090 * * 1100 * * 1110 * * 1120 * * 1130 * * 1140 * *
SEQ03_ORF CCACCCAGGC CAGCAAGTCA TCCACAGGCT TCTTTTAATC TGGCCAGTCC TGAGAAGGTC
GGTGGGTCCG GTCGTTCAGT AGGTGTCCGA AGAAAATTAG ACCGGTCAGG ACTCTTCCAG

1150 * * *
SEQ03_ORF AGTAATACAA CTGTAGTA
TCATTATGTT GACATCAT



EXHIBIT C

	10	20	30	40	50	60	
	*	*	*	*	*	*	
SEQ05_ORF	ATGGAAAGGC	ATTTGCTCAC	GGTTCAGAA	GCTGTAGTT	CTGGGTCTGG	TAATGAAGTC	
	TACCTTCCG	TAAACGAGTG	CCAAGGTCTT	CGACATCCAA	GACCCAGACC	ATTACTTCAG	
	250	260	270	280	290	300	
Marra EST	cTGGctgtGC	tggTcaTCct	GGc-tCAGct	--gacAGcTT	CcGGaTCcaG	TtATcAgaTC>	
SEQ05_ORF	ATGGAAAGGC	ATTTGCTCAC	GGTTCAGAA	GCTGTAGTT	CTGGGTCTGG	TAATGAAGTC	
	70	80	90	100	110	120	
	*	*	*	*	*	*	
SEQ05_ORF	ATAGAAGGCC	CCCAGAAATGC	AACAGTCCTG	AAGGGCTCCC	AGGCTCGTT	CAACTGCACC	
	TATCTTCCGG	GGGTCTTACG	TTGTCAAGGAC	TTCCCAGGG	TCCGAGCGAA	GTGACGTGG	
	310	320	330	340	350	360	
Marra EST	ATAGAAGGtC	CtCAGAAATGt	AACAGTCCTa	AAGGAGTCAG	AGGCTCaCTT	CAACTGCACC>	
SEQ05_ORF	ATAGAAGGCC	CCCAGAAATGC	AACAGTCCTG	AAGGGCTCCC	AGGCTCGTT	CAACTGCACC	
	130	140	150	160	170	180	
	*	*	*	*	*	*	
SEQ05_ORF	GTCTCCCAGG	GCTGGAAGCT	CATCATGTGG	GCTCTCAGTG	ACATGGTGGT	GCTAAGCGTC	
	CAGAGGGTCC	CGACCTTCGA	GTAGTACACC	CGAGAGTCAC	TGTACCACCA	CGATTCGCAG	
	370	380	390	400	410	420	
Marra EST	GTgaCtCACG	GCTGGAAGCT	tcTCATGTGG	aCTCTtAacc	AaATGGTGGT	GCTgAGtcTC>	
SEQ05_ORF	GTCTCCCAGG	GCTGGAAGCT	CATCATGTGG	GCTCTCAGTG	ACATGGTGGT	GCTAAGCGTC	
	190	200	210	220	230	240	
	*	*	*	*	*	*	
SEQ05_ORF	AGGCCCATGG	AGCCCATCAT	CACCAATGAC	CGCTTCACCT	CTCAGAGGTA	CGACCAGGGC	
	TCCGGGTACC	TCGGGTAGTA	GTGGTTACTG	CGGAAGTGGG	GAGTCTCCAT	GCTGGTCCCG	
	430	440	450	460	470	480	
Marra EST	ccaCCCAGG	-aCCCATCAT	CACCAACaAC	CGtTTCACCT	aTgcccAGtTA	-cAaCAGcat>	
SEQ05_ORF	AGGCCCATGG	AGCCCATCAT	CACCAATGAC	CGCTTCACCT	CTCAGAGGTA	CGACCAGGGC	
	250	260	270	280	290	300	
	*	*	*	*	*	*	
SEQ05_ORF	GGGAACATTCA	CCTCGGAGAT	GATCATCCAC	AATGTGGAGC	CCAGTGATTG	GGGAAACATC	
	CCCTTGAAAGT	GGAGCCTCTA	CTAGTAGGTG	TTACACCTCG	GGTCACTAAG	CCCCTTGAG	
	490	500	510	520			
Marra EST	GacAgCTTCA	tCTCGGAGtT	GATCATCCAt	gATGTGcAGC	CCAGTG>		
SEQ05_ORF	GGGAACATTCA	CCTCGGAGAT	GATCATCCAC	AATGTGGAGC	CCAGTG		

	310	320	330	340	350	360	
SEQ05_ORF	*	*	*	*	*	*	*
	370	380	390	400	410	420	
SEQ05_ORF	*	*	*	*	*	*	*
	430	440	450	460	470	480	
SEQ05_ORF	*	*	*	*	*	*	*
	490	500	510	520	530	540	
SEQ05_ORF	*	*	*	*	*	*	*
	550	560	570	580	590	600	
SEQ05_ORF	*	*	*	*	*	*	*
	610	620	630	640	650	660	
SEQ05_ORF	*	*	*	*	*	*	*
	670	680	690	700	710	720	
SEQ05_ORF	*	*	*	*	*	*	*
	730	740	750	760	770	780	
SEQ05_ORF	*	*	*	*	*	*	*
	790	800	810	820	830	840	
SEQ05_ORF	*	*	*	*	*	*	*
	850	860	870	880	890	900	
SEQ05_ORF	*	*	*	*	*	*	*

